CLAIMS

That which is claimed is:

1. A method for detecting a predisposition to a disorder in a subject caused by an alteration in hypocretin receptor activity, the method comprising:

analyzing nucleic acid of a subject for the presence of at least one polymorphism that predisposes the subject to a disorder caused by an alteration in activity of a hypocretin receptor;

wherein the presence of the predisposing polymorphism is indicative of an increased susceptibility of the subject to a disorder caused by an alteration in a hypocretin receptor activity.

2. The method of claim 1, wherein the predisposing polymorphism is in a hypocretin receptor gene.

3. The method of claim 1, wherein the predisposing polymorphism is in a hypocretin receptor-2 gene.

4. The method of claim 1, wherein the predisposing polymorphism is in a hypocretin polypeptide.

5. The method of claim 1, wherein the disorder is a sleep disorder.

6. The method of claim 5, wherein the predisposing polymorphism causes a sleep disorder characterized by decreased wakefulness.

7. The method of claim 5, wherein the predisposing polymorphism causes a sleep disorder characterized by increased wakefulness or insomnia.

8. The method of claim 5, wherein the disorder is narcolepsy.

9. The method of claim 1, wherein the disorder is selected from the group consisting of a mood disorder, chronic fatigue syndrome and an attention deficit disorder.

10. The method of claim 1, wherein the subject is human.

11. The method of claim 1, wherein the subject is canine.

12. The method of claim 11, wherein the polymorphism to be detected is within a genomic region between markers 26-8 and 530-3, inclusive, of canine chromosome 12.

13. A method of screening for biologically active agents that modulate sleep or wakefulness through modulation of hypocretin receptor activity, the method comprising:

combining a candidate agent with an isolated cell comprising a nucleic acid encoding a mammalian hypocretin receptor polypeptide;

determining the effect of said agent on hypocretin receptor activity;

wherein an agent that modulates hypocretin receptor activity and thus modulates sleep or wakefulness is identified where the agent increases or decreases hypocretin receptor activity.

14. The method of claim 13, wherein the candidate agent is a hypocretin receptor agonist and hypocretin receptor activity is detected by binding of the candidate agent to the hypocretin receptor.

15. The method of claim 13, wherein the agent is a hypocretin receptor antagonist and hypocretin receptor activity is detected by .

16. A method of screening for biologically active agents that modulate sleep or wakefulness through modulation of hypocretin receptor activity, the method comprising:

administering a candidate agent to a non-human animal model for function of an hypocretin receptor gene, the animal comprising a genetic alteration of a hypocretin receptor gene sequence or a hypocretin polypeptide sequence;

determining the effect of said agent on hypocretin receptor activity;

wherein an agent that modulates hypocretin receptor activity and thus modulates sleep or wakefulness is identified where the agent increases or decreases hypocretin receptor activity.

17. The method of claim 16, wherein said determining is by detecting an alteration in sleep pattern in the animal.

18. A method of treating a sleep disorder in a subject, the sleep disorder being characterized by decreased wakefulness relative to an unaffected subject, the method comprising:

administering to a subject having a sleep disorder associated with decreased wakefulness an amount of a hypocretin receptor agonist effective to increase wakefulness in the subject.

19. The method of claim 18, wherein the hypocretin receptor agonist is hypocretin or a hypocretin derivative.

20. The method of claim 18, wherein the sleep disorder is narcolepsy.

21. A method of treating a sleep disorder in a subject, the sleep disorder being characterized by increased wakefulness relative to an unaffected subject, the method comprising:

administering to a subject having a sleep disorder associated with increased wakefulness an amount of a hypocretin receptor antagonist effective to increase sleep in the subject.

22. A method of treating a subject having a hypocretin system disorder that causes at least one of depression, chronic fatigue syndrome or attention hyperactivity disorder, the method comprising:

administering to the subject an amount of a hypocretin receptor agonist sufficient to alleviate symptoms of the hypocretin system disorder.

23. A method for predicting the responsivity of a subject to administration of an agonist or antagonist of hypocretin receptor, wherein the subject suffers from a disorder selected from the group consisting of a sleep disorder, a mood disorder, chronic fatigue syndrome or an attention deficit disorder, the method comprising:

analyzing the genomic DNA or mRNA of a subject for the presence of at least one polymorphism selected from the group consisting of: a hypocretin receptor polymorphism and a hypocretin peptide polymorphism;

wherein the presence of the polymorphism indicates an increased probability that the subject suffers from a disorder that can be treated by administration of a hypocretin receptor agonist or hypocretin receptor antagonist.

24. A pharmaceutical composition comprising a hypocretin receptor agonist in an amount effective to promote wakefulness.

25. The pharmaceutical composition of claim 24, wherein the hypocretin receptor agonist is hypocretin or a hypocretin derivative.

26. A pharmaceutical composition comprising a hypocretin receptor antagonist in an amount effective to promote sleep.

27. A method for detecting a predisposition to a sleep disorder in an individual, the method comprising:

detecting an autoimmune response in a biological sample from a subject suspected of having or being susceptible to a sleep disorder, wherein the autoimmune response causes a decrease in

binding of endogenous hypocretin to a hypocretin receptor or leads to destruction of hypocretin producing cells;

wherein detection of the autoimmune response is indicative of a sleep disorder in the subject.

28. The method of claim 27, wherein the autoimmune response is detected by detecting the presence of an auto antibody that specifically binds a hypocretin receptor.

29. The method of claim 27, wherein the autoimmune response is a cellular immune response is directed against a hypocretin receptor.

30. The method of claim 27, wherein the autoimmune response is directed against a component of a hypocretin-containing cell.

31. The method of claim 27, wherein the sleep disorder is narcolepsy.

32. A method for detecting a sleep disorder or a predisposition to a sleep disorder in an subject, the method comprising:

detecting a level of hypocretin in a biological sample from a test subject suspected of having or being susceptible to a sleep disorder;

wherein detection of a level of hypocretin in the sample that is altered relative to a level of hypocretin in a normal subject is indicative of a sleep disorder in the test subject.

33. The method of claim 32, wherein said detecting is by detection of binding of hypocretin-binding molecule to hypocretin in the test sample.

34. The method of claim 32, wherein said detecting is by detection of a biological activity of a peptide derived from the preprohypocretin gene.

35. The method of claim 32, wherein said detecting is by detection of an amount of hypocretin peptide in the sample.

36. The method of claim 32, wherein the sleep disorder is narcolepsy.

37. A method for detecting a hypocretin-related disorder or susceptibility to a hypocretin-related disorder in a subject, the hypocretin-related disorder being selected from the group consisting of a mood disorder, chronic fatigue syndrome, and attention deficit disorder, the method comprising:

detecting at least one of: a) a level of hypocretin peptide in a sample from a test subject, b) a level of expression of a hypocretin receptor in a sample obtained from a test subject, or c) a number of hypocretin-containing cells in tissue of a test subject, wherein the test subject is suspected of suffering from a hypocretin-related disorder;

wherein detection of a level of hypocretin peptide, a level of hypocretin receptor expression, or a number of hypocretin-containing cells that is altered relative to that found in a normal subject is indicative of a hypocretin-related disorder in the test subject.

38. An isolated nucleic acid molecule comprising at least 15 contiguous nucleotides and capable of hybridizing under high stringency conditions to a sequence encoding a mutated canine hypocretin receptor or a complement of said sequence encoding a mutated canine hypocretin receptor, which mutated hypocretin receptor causes canine narcolepsy.

39. The isolated nucleic acid molecule of claim 38, wherein the probe hybridizes specifically to a sequence encoding an amino acid having a sequence of SEQ ID NO:10.

40. The isolated nucleic acid molecule of claim 38, wherein the probe hybridizes specifically to a sequence encoding an amino acid having a sequence of SEQ ID NO:11.

41. The isolated nucleic acid molecule of claim 38 further characterized by specific hybridization to SEQ ID NO:13.

42. The isolated molecule of claim 38 further characterized by specific hybridization to SEQ ID NO:15.

43. A kit comprising the isolated nucleic acid molecule of claim 38, wherein the kit is useful in detecting a narcolepsy susceptibility locus in a canine subject.

44. A kit for use in detection of a canine narcolepsy susceptibility locus, the kit comprising at least one primer for amplification of a narcolepsy informative region, wherein the primer is selected from the group consisting of SEQ ID NOS:32-53.

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